# Slow Heart Rates and Increased Risk of Cardiac Death in Middle-Aged Men

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**Sustained slow heart rates in men of middle age or older who have coronary heart disease, hypertension, or pulmonary disease may be evidence of underlying disease of the cardiac pacemaker and of increased risk of sudden cardiac death. In a seven-year prospective study of 301 men, those whose mean heart rates did not rise as expected during a day's activities, who had a low peak rate response to standard exercise, and who showed little evidence of phasic variation in heart rate with respiration, and no evidence of the random abrupt sinus slowing that occurs with sighing, coughing, or straining, often had overt abnormalities of their cardiac pacemakers (eg, wandering atrial pacemaker, atrioventricular [A-V] junctional rhythm, "coronary sinus rhythm") or developed these later. They experienced significantly more sudden cardiac deaths than expected ($P < .005$).**

This paper describes the occurrence of sustained slow heart rates in active middle-aged men and considers their relation to disorders of the cardiac pacemaker and conduction system and to subsequent cardiac death. The findings are based upon a seven-year prospective study of a random sample of 301 steadily employed middle-aged men. The asymptomatic disturbances of rhythm and conduction which were found among these men and the relation of these to preexisting or subsequently developing coronary heart disease have been described in a previous paper.[1]

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## Methods

Subjects for the study were selected with the intention of obtaining a probability sample of actively employed and ostensibly healthy American men who could be studied intensively, and followed over a period of years, at an age when a high incidence of new events of coronary heart disease and of cardiac death could be expected. The sample consisted of 301 men between the ages of 55 and 60 years who were on the active payroll of the New Jersey Bell Telephone Company on Jan 1, 1962. The demographic characteristics of the population of Bell system employees, from which this sample was drawn, have been studied extensively.[2-5] The incidence of coronary heart disease in this population was closely similar to the incidence of this disease among all employed American men at the time when this study was carried out. The subjects were randomly designated from the group of all men in their age cohort who were then on the payroll of the company. The sample was stratified so as to insure adequate representation of all major occupational categories. The methods used in the sampling have been described.[4]

At the time of intake, the subjects were examined and studied in terms of their physical characteristics, their electrocardiograms, chest roentgenograms, serum lipid levels, dietary histories, habits, activities, and psychological and social characteristics. From each man we obtained a sample of 20,000 to 30,000 cardiac complexes by recording his electrocardiogram continuously over a six- to seven-hour period of carefully standardized activities, which were carried out between 8:30 AM and 4:30 PM. The routine included various changes of position, graded levels of physical activity, and exposure to the effects of ingesting hot and cold fluids, or eating a large meal, and of taking part in interviews and psychological tests which were anxiety producing for some men. The electrocardiographic data were obtained with portable tape recorders (the Holter Avionics' "Electrocardiocorder")[6] after the voltage and timing characteristics of these devices had been ascertained and after arrangements had been made to offset some of the inherent limitations of this

equipment.[7] The routine that the men carried out was timed and guided by technicians who accompanied them.

In order to analyze the data from the cardiac recording, a complete photographic write-out of the R-R intervals was prepared[7] on which the time of each activity was precisely located. From this record heart rates under various conditions were calculated, and potential changes in rhythm and potential dysrhythmias were identified. These were investigated by scanning the records at real-time and by the real-time write-out of the complexes.

The examination of the men and the initial collection of the electrocardiographic data were complete in 1963 and 1964. After that, the group was followed and information was obtained about all deaths and all periods of disability that occurred. The subjects were reexamined beginning in 1967. On this occasion, their electrocardiograms were recorded over a 24-hour period, which yielded samples of approximately 120,000 complexes. The longer records were obtained after it had become evident from other studies that important phenomena of heart rate, rhythm, and conductions might occur in the evening and during the course of sleep.

The second examinations were completed in December of 1969. Some men could not be examined for a second time because they were disabled or because they had moved away from the area, or for other reasons. These men were contacted by telephone and their interval histories were reviewed with them. It was arranged that those who were nearby would have electrocardiograms and records of their blood pressures obtained at their homes by our technicians. Men living in other states had electrocardiograms and blood pressure measurements performed by their private physicians, who were contacted by us, instructed in our methods of carrying out these procedures, and paid a small fee for their services.

## Results

**Recordings Obtained.**—At the initial examination 283 complete records suitable for analysis were obtained. Incomplete or partly defective records were obtained from most of the remaining subjects (Table 1). At follow-up, information was obtained on the condition of all of the men in the original sample. Two hundred-fourteen men (71.7% of those originally examined) returned for a second complete examination and 24-hour recording. Twenty-seven men died before they could be reexamined. Sixty men could not be reexamined—20 because they were disabled and unable to make the trip to New York, 11 because they had moved to other parts of the country, and 25 for "personal reasons"—chiefly because their wives or other members of their families were disabled and they had no one to leave them with, or because they themselves thought that the trip to New York and a day of examination would cause them too much discomfort or inconvenience.

All except four of these men reviewed their interval histories with us and allowed us to obtain blood pressure readings and electrocardiograms. In four instances we could obtain data only from the health record of the man until he retired from the company, and we knew that he was still alive at the time that this report was prepared.

**Prevalence of Cardiovascular, Pulmonary, and Metabolic Abnormalities at the Time of the First Examination.**—At the time of the original examination, the sample was found to include 66 men with clinical evidence of "definite" or "probable" arteriosclerotic ("coronary") heart disease (Table 2). Twenty-nine of these men had definite overt coronary heart disease according to the Princeton Conference Criteria[8]: they had had previous myocardial infarctions, typical angina pectoris, previous episodes of acute coronary insufficiency, or definite electrocardiographic evidence of a previous myocardial infarction (QRS criteria). Twenty-seven other men, who had otherwise unexplained abnormalities of their ST segments 1.0 mm or greater in magnitude, or diphasic or inverted T-waves on the standard electrocardiogram, or who had somewhat atypical symptoms which were regarded by the examining physician as "probable angina pectoris," were considered to have "probable coronary heart disease." (Eight men, who were previously classified in a "high risk" or a "medium risk" group[1] were transferred to this group after a careful review of the original clinical data suggested that the prior classification had been too conservative.)

There were 99 men who were considered to have definite vascular hypertension, with or without clinical evidence of hypertensive heart disease. These men had blood pressures of 160/95 mm Hg or greater (the mean of two readings in both arms), or they had the left ventricular hypertrophy (LVH) pattern on the ECG, or left ventricular enlargement by roentgenogram (cardio-thoracic ratio equal to or greater than 50%). Seventy-seven other men, with blood pressures of 140 to 159/90 to 94 mm Hg, were considered to have "borderline hypertension."

There were 68 men with clinical evidence of pulmonary disease. Twenty-nine men were classified as having "definite pulmonary disease." Each of them had a clear-cut clinical history, with supporting physical findings (deformity of the chest, impaired respiration, cough, rhonchi, rales, or diminished breath sounds), often with abnormalities visible on the roentgenogram. They included 7 men with roentgenographic evidence of old inflammatory disease accompanied by fibrosis, bullous emphysema, or bronchitis; 1 man with a history and findings consistent with bronchial asthma; 20 men with histories and findings consistent with chronic bronchitis or obstructive emphysema, or both; and 1 man with a previously undiagnosed carcinoma of the lung. Thirty-nine men, with "probable pulmonary disease," had either clearcut clinical histories or highly suggestive findings on examination or roentgenogram. They included 31 men with probable chronic bronchitis or emphysema, or both, 6 men with asthma, and 2 men with old inflammatory disease and fibrosis.

There were 8 men in the sample who had coronary heart disease and hypertension as well as pulmonary disease, and there were 38 men who

**Table 1.—Follow-up Information Obtained**

| | No. | % of Total |
|---|---|---|
| Initial examination, 1963-1964 | | |
| Men examined | 301 | 100 |
| Complete recordings | 283 | 94.0 |
| No. of complexes/complete recording | 30,272 ± 644.8 | |
| Died before second examination | 27 | 9.0 |
| Second examination, 1967-1969 | | |
| Examined completely with 24-hour recordings | 214 | 71.7 |
| Interval history, standard ECG and blood pressure only | 56 | 18.6 |
| Data from company only | 4 | 1.3 |
| Died before second examination but before May 1971 | 20 | 6.6 |

**Table 2.—Prevalence of Several Cardiovascular, Pulmonary, and Metabolic Conditions at the Initial Examination***

| | No. of Men | | Rate per 100 | |
|---|---|---|---|---|
| 1. Clinical evidence of arteriosclerotic ("coronary") heart disease | | | | |
| *a*. "Definite" | 39 | | 13.0 | |
| *b*. "Probable" | 27 | | 9.0 | |
| Total men with *a* or *b* | | 66 | | 21.9 |
| 2. Vascular hypertension, regardless of etiology | | | | |
| *a*. Definite (≥160/95) | 92 | | 30.6 | |
| *b*. "Borderline" (140-159/90-94) | 77 | | 25.6 | |
| *c*. LVH pattern on ECG | 21 | | 7.0 | |
| *d*. Left ventricular enlargement on roentgenogram | 5 | | 1.7 | |
| Total men with *a*, *c*, or *d* | | 99 | | 32.9 |
| 3. Clinical evidence of pulmonary disease, all forms | | | | |
| *a*. Definite | 29 | | 9.6 | |
| *b*. Probable | 39 | | 13.0 | |
| Total men with *a* or *b* | | 68 | | 22.6 |
| 4. Men without 1, 2 (*a*, *c*, or *d*) or 3 | 126 | | 41.9 | |

* For criteria, see text. LVH = left ventricular hypertrophy.

had combinations of two of these three conditions. There were 126 men who had no definite evidence of any of these three conditions, although many of these had minor ST and T-wave abnormalities, borderline hypertension, or suggestive evidence of pulmonary disease.

Some of the physical and social characteristics of the men in the sample and some of their habits and activities have been described in various publications.[2-5] As a group they were men of heavy build. Their mean ponderal index was 12.34 ± 0.06 (variation expressed as two times the standard error of the mean). Sixty-three of them had ponderal indices of less than 12.00 and 103 of them were described as "clinically obese" by the physicians who examined them. Their mean cholesterol concentration was 249.2 ± 4.7 mg/100 ml. Twenty of them had cholesterol levels of 300 mg/100 ml or higher. Fifty-five had serum uric acid levels greater than 7.0 mg/100 ml, and 20 had diabetes mellitus. All except 40 had smoked at some time during their lives. Two hundred-eight had smoked for 30 years or more, 69 were still smoking a pack of cigarettes a day, and 27 were smoking at a rate of two packs a day or more. They engaged in relatively little physical exercise and in almost no heavy physical work. Their mean daily caloric expenditure from all physical activities, as estimated from the Passmore and Durnin tables[9] was 2,920 ± 39 kilogram calories. The group included 79 workmen, 46 foremen, 86 supervisors, and 90 managers and executives.

**Heart Rates.**—The standard procedure that was utilized made it possible to study the heart rates of these men over a six-hour period of the morning and early afternoon, and to compare the findings from man to man. Each man spent two minutes in the supine, left lateral, right lateral, standing, sitting, and knee-chest positions. He then performed a Valsalva maneuver. Following this, he performed a standard two-step test according to the specifications of Master.[10] Next he consumed a "breakfast" consisting of 500 ml of ice water, which he drank rapidly, and followed, after an interval of several minutes, by 500 ml of hot coffee. This was usually accompanied by the eating of two pieces of toast. Some ten minutes after breakfast ended, he walked out-of-doors 175 meters to a nearby office. During the next hour he sat at a table performing standard paper and pencil psychological tests. According to the estimate of the psychologist, these tests produced moderate anxiety in some of the men. After a brief interval, he underwent one hour of interview with a sociologist. This interview also aroused moderate anxiety in some men. The subject then walked, out-of-doors, 125 meters to a cafeteria, where he consumed a meal consisting of an appetizer, soup, meat, vegetables, potatoes, a dessert (pie or ice cream), and 360 ml of a sweetened carbonated beverage. Immediately after the meal he walked up a flight of 13 stairs and 125 meters out-of-doors to return to the office. There he again sat at a table performing psychological tests or filling out questionnaires for about two hours, at which point the recorder was removed. The procedure began between 8:30 and 9:00 AM and lasted until 3:00 to 3:30 PM. If the subject wished to smoke during the period of recording, he was allowed to do so. Defecation, if necessary, was allowed during the pe-

riod of the recording. At the end of the recording, most subjects described themselves as "tired."

The electrocardiogram was recorded continuously during the routine. Heart rates which were made the subject of a special study were the following:

1. The morning supine rate—the mean rate during one minute with the subject in a supine position, fasting, about 8:30 AM, shortly after the recorder had been attached;
2. Preexercise rates—the mean rate during one minute with the subject seated:
   a. Immediately before the standard exercise test (about 9 AM, fasting),
   b. Immediately before the "175-meter walk" (about 9:45 AM, 10 minutes after the "breakfast"), and
   c. Immediately before the "stairs and 125-meter walk" (about 1 PM, after the ingestion of the noon meal);
3. Maximum rates during exercise: peak rates attained during exercise periods;
4. Rates two, five, and ten minutes after each exercise period ended;
5. Mean morning rate—mean rates during ten random minutes during two hours of sedentary activity in the morning, approximately from 10 AM to 12 noon;
6. Prelunch rates: mean heart rates during one minute with the subject seated, immediately before eating lunch (shortly after 12 noon);
7. Postlunch rates: mean rate with subject seated immediately after ingesting the noon meal (shortly before 1 PM); and
8. Mean afternoon rate: mean rate during ten random minutes during two hours of sedentary activity in the afternoon (approximately 1:15 to 3:15 PM).

In the morning as they lay supine at the beginning of the recording, the mean heart rate of the men in the sample was 66.4 ± 1.38 (2 standard error of the mean [SEM]). During the morning period of sedentary activity their mean heart rate was 77.12 ± 1.52. By the end of the morning, at the beginning of the large lunch, the mean heart rate had risen to 84.1 ± 1.71, and at the end of the lunch it was 86.4 ± 1.67. During the period of sedentary activity in the early afternoon, it was 91.8 ± 1.78. There was a mean rise of 25.4 beats per minute from the initial supine rate to the mean afternoon rate (Fig 1).

The morning supine heart rates were the slowest sustained heart rates that were recorded at any time during the day. They were not necessarily a good indicator of the heart rate during the remainder of the day. Many men who had a bradycardia at this time had normal heart rates during the rest of the day, and some went on to develop a sustained tachycardia. The heart rate obtained from the standard electrocardiogram was an even less reliable indicator of the general level of heart rates during the rest of the day. There were 21 men who had a bradycardia when their standard electrocardiograms were being taken but at no other time during the day. Apparently these men, when asked to lie still, held their breath and carried out, in effect, a Valsalva maneuver.

With each of the brief periods of exercise, the heart rate of the men rose modestly—to 112.6 ± 2.7 during the standard exercise test, to 108.2 ± 1.77 during the morning walk, and to 121.6 ± 1.93 during the stair climb and walk after lunch. After each period of activity, the rate returned within ten minutes to levels five or six beats higher than the baseline (Fig 1).

**Subsequent Cardiac Deaths.**—In the seven years after the examination, up to May 1971, 47 men in the sample died. Twenty-six of these men were reported on their death certificates as having died with manifestations of arteriosclerotic heart disease—chiefly "acute myocardial infarction." The clinical and autopsy data relating to these deaths were obtained and reviewed, and interviews were carried out with physicians, relatives, and observers of the deaths.

The clinical characteristics of the fatal episodes of 14 of these 26 men were those of an abrupt and unexpected death in a man who had not appeared to be acutely ill a few moments before the episode began (Table 3). At one moment in time, these men were busy with their usual activities; minutes later they had collapsed and died. Eight other men died during the course of illnesses having the clinical characteristics of an acute myocardial infarction. One died during the course of an acute exacerbation of chronic congestive heart failure. Another died in a setting of acute respiratory failure, and two died unobserved and unexpectedly in their beds, whether abruptly or gradually is not known. It was our estimate that probably 18 of these men died because of the development of a dysrhythmia or cardiac standstill. Four others apparently died of pump failure, and four may have died in either manner.[11]

Thirteen of the 26 men who were reported as dying of coronary heart disease had clinical coronary heart disease (Princeton Conference Criteria) at the time of their first examination. Three others developed clinical coronary heart disease before their fatal episode. All of the 26 had definite clinical evidence of either coronary heart disease, hypertension, or chronic pulmonary disease, or a combination of these conditions, at the time of their last examination before their deaths.

Ten of the 26 were men whose primary diagnosis at the time of their last examination was coronary heart disease; five of these men with coronary heart were obese or diabetic, or both. Three other men had coronary heart disease and chronic bronchitis and emphysema, and two of these were obese.

Three men, whose primary diagnosis was hypertensive cardiovascular disease, also had some evidence of coronary heart disease; one of these three was obese, one was a diabetic, and two had chronic bronchitis and emphysema. Three others were men whose primary illness appeared to be hypertensive cardiovascular disease and LVH, essentially uncomplicated. One man was hypertensive but also

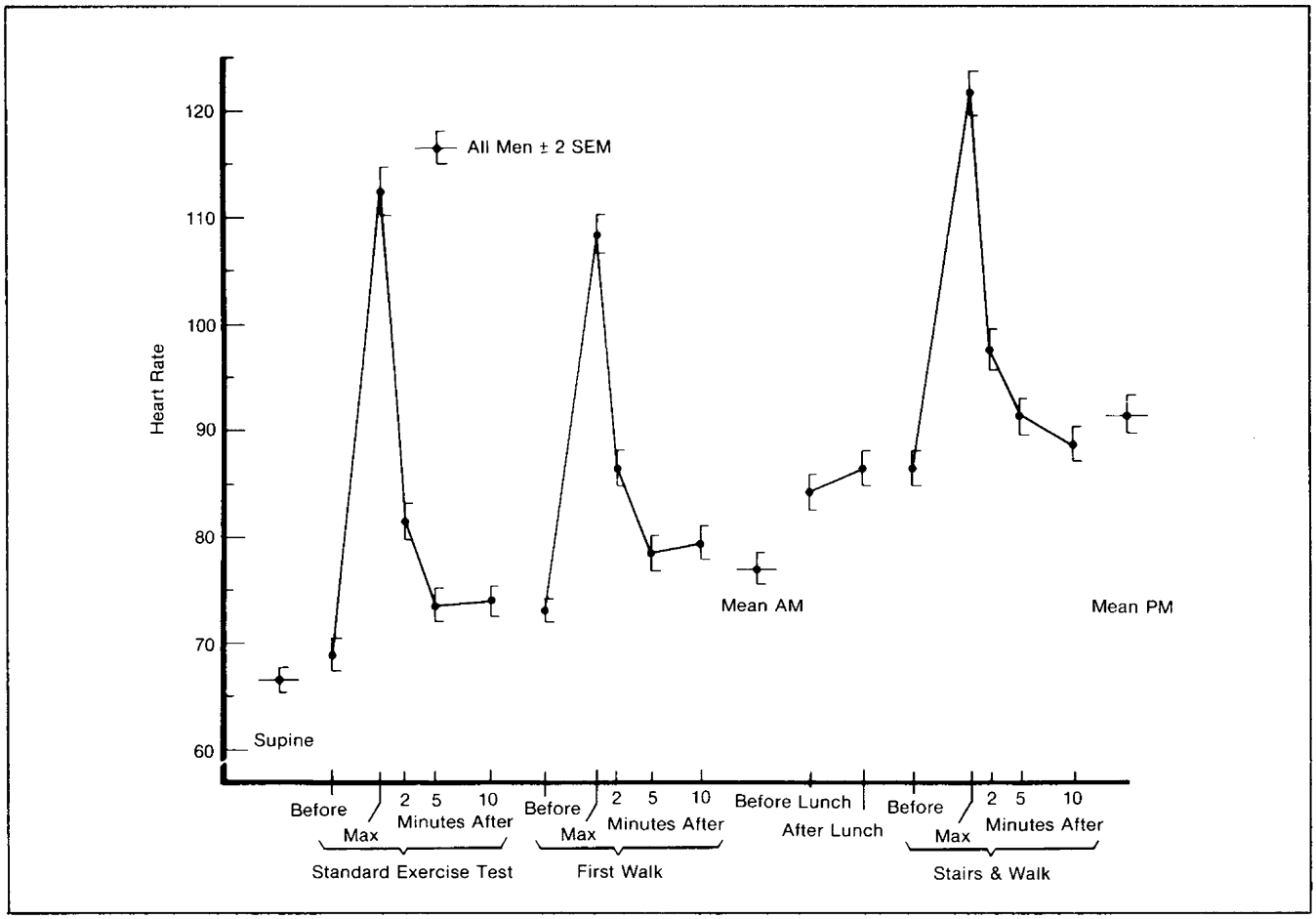


Fig 1.—Diagrammatic representation of the mean heart rates of the subjects during the six-hour standardized routine of activities.

had some emphysema.

Five of the 26 men had a primary diagnosis of chronic lung disease at the time of the last examination. One of these may have been concealing angina pectoris, one was an alcoholic, two were obese, two were diabetic, and one probably had cor pulmonale.[11]

Twenty-one men were reported on their death certificates as dying of causes other than coronary heart disease (Table 4). Five of these men died with cardiovascular conditions—two had strokes, one had bacterial endocarditis, and two who had cancer died in cardiac failure. One man died of emphysema, one died of cirrhosis of the liver, and fifteen died primarily of cancer—including six with cancer of the lung, and two with cancer of the urinary bladder. Three of the 21 men in this group had definite coronary heart disease at the time of their last examination before death, and one had ischemic ST segments on his standard electrocardiogram; eight had definite hypertension, including two with left ventricular enlargement (LVE) on roentgenogram and one with LVH on the ECG. Five had emphysema or chronic bronchitis. All except one had smoked for 30 years; six were smoking two or more packs of cigarettes per day when they were last examined.

**Heart Rates and Subsequent Cardiac Death.**—The 26 men reported as dying of "coronary heart disease" were found to have had consistently slower heart rates than the other men in the sample at the time of the first examination (Fig 2). Excluding one man who died in a setting of acute respiratory failure, two men whose deaths were not observed, and one man for whom no rate data were available, there were 22 men who experienced "coronary deaths" for whom rate data were available. Among these men there were six with morning supine rates faster than 70 beats per minute. There were ten men with mean morning rates of 70 beats per minute or lower, and seven men with mean afternoon rates of 80 beats per minute or lower. There were seven men whose mean afternoon rates were not more than 15 beats per minute higher than the morning supine rates. During the morning walk, seven of these men did not attain heart rates higher than 99 beats per minute, and during the stair climb

**Table 3.—Twenty-six Deaths Reported as "Coronary Deaths": Prior Clinical Findings and Nature of Fatal Episode***

| Code No.* | Preexisting Clinical Disease: Cardiovascular Heart | Preexisting Clinical Disease: Hypertensive | Preexisting Clinical Disease: Pulmonary | Sustained Relative Bradycardia | Clinical Character of Fatal Episode | Nature of Death | Estimated Mechanism of Death |
|---|---|---|---|---|---|---|---|
| 87 | MI, CI, AP | — | — | — | Acute MI | Gradual—hours | Pump failure |
| 120 | MI | — | — | (Almost) | Acute MI | Gradual—1 hr | Pump failure |
| 138 | MI, CI, AP | Definite | — | SRB | Acute MI | Abrupt—after 3 hr | Arrhythmia |
| 141 | MI | Borderline | — | — | Sudden death | Abrupt—minutes | Arrhythmia |
| 157 | MI, AP | Borderline | — | SRB | Sudden death | Abrupt—minutes | Arrhythmia |
| 327 | MI | ? | Emphysema | — | Sudden death | Abrupt—minutes | Arrhythmia |
| 21 | CI, AP | Borderline | — | — | Acute MI | Abrupt—after 1 day | Arrhythmia |
| 48 | CI, AP | Definite LVE | — | — | Sudden death | Abrupt—minutes | Arrhythmia |
| 89 | CI, AP | Definite LVH | Emphysema bronchitis | SRB | Congestive heart failure | Abrupt—after 4 days | Arrhythmia |
| 259 | CI, AP | Definite LVH | Chronic bronchitis | — | Acute MI | Abrupt—after 1 day | Arrhythmia |
| 328 | AP | — | Chronic bronchitis | — | Sudden death | Abrupt—minutes | Arrhythmia |
| 332 | ECG | Borderline | — | — | Acute MI | Gradual—4 hr | Pump failure |
| 343 | AP | Definite | Emphysema | — | Acute MI | Gradual—½ hr | Pump failure |
| 30 | — | — | Emphysema | — | Acute respiratory failure | Gradual—hours | Pump failure |
| 115 | — | Definite LVH | — | SRB | Sudden death | Abrupt—minutes | Arrhythmia |
| 135 | — | Definite LVH | — | SRB | Acute MI | Gradual—1 hr | Pump failure |
| 55 | — | — | Emphysema | — | Sudden death | Abrupt—minutes | Arrhythmia |
| 92 | MI, AP | Borderline | — | — | Sudden death | Abrupt—minutes | Arrhythmia |
| 221 | — | Borderline | Emphysema | — | Unknown-? sudden | Less than 1 day | Unknown |
| 28 | ECG | Borderline | — | SRB | Sudden death | Abrupt—minutes | Arrhythmia |
| 31 | AP | Definite | — | — | Sudden death | Abrupt—minutes | Arrhythmia |
| 73 | — | Borderline | Emphysema bronchitis | (Almost) | Sudden death | Abrupt—minutes | Arrhythmia |
| 101 | — | Definite LVH | — | SRB | Sudden death | Abrupt—minutes | Arrhythmia |
| 275 | — | — | Emphysema bronchitis | SRB | Sudden death | Abrupt—minutes | Arrhythmia |
| 303 | — | Definite | Chronic bronchitis | — | Sudden death | Abrupt—minutes | Arrhythmia |
| 334 | — | Borderline LVE | Emphysema bronchitis | — | Unknown-? sudden | Less than 12 hr | Unknown |

* MI = myocardial infarction, CI = coronary insufficiency, AP = angina pectoris, LVH = left ventricular hypertrophy, and LVE = left ventricular enlargement on roentgenogram.

† The code numbers in this and subsequent tables are listed in the order in which the "risk of coronary death" of the men was estimated at the first examination, with the men in the "lowest risk" groups at the bottom.[1]

and walk after lunch, four of them failed to attain rates of 99 beats per minute. Of the 15 men in the group who participated in the morning exercise tolerance test, three failed to attain maximum heart rates greater than 99 beats per minute.

Because of the frequency of slow heart rates among the men who subsequently experienced acute "coronary deaths," we investigated the relation of slow heart rates to subsequent cardiac death.

Seven phenomena of slow heart rate were considered: (1) morning supine rate ≤ 60 beats per minute; (2) a mean morning rate ≤ 70 beats per minute; (3) a mean afternoon rate ≤ 80 beats per minute; (4) a rate rise from the morning supine rate to the mean afternoon rate ≤ 15 beats per minute, provided the morning supine rate was 70 beats per minute or less; and (5), (6), and (7), a maximum heart rate during each of the three exercise periods of ≤ 99 beats per minute. A man who exhibited any one of these phenomena had a heart rate 2 standard errors or more below the mean heart rate for all of the men in the sample for the particular rate being considered. There were 139 men who exhibited one or more of these phenomena of slow heart rate. Subsequently there were 2.5 more deaths than expected among this group (not significant). (Except when it is otherwise stated, probabilities are based on findings of the $\chi^2$ test. NS = $P > .1$.)

On a categorical basis, there were found to be three phenomena of slow heart rate which were significantly associated with subsequent acute "coronary death": (1) a mean afternoon heart rate less than 80 beats per minute ($P = .05$); (2) a mean afternoon heart rate not more than 15 beats per minute greater than the morning supine rate, provided the morning supine rate was not greater

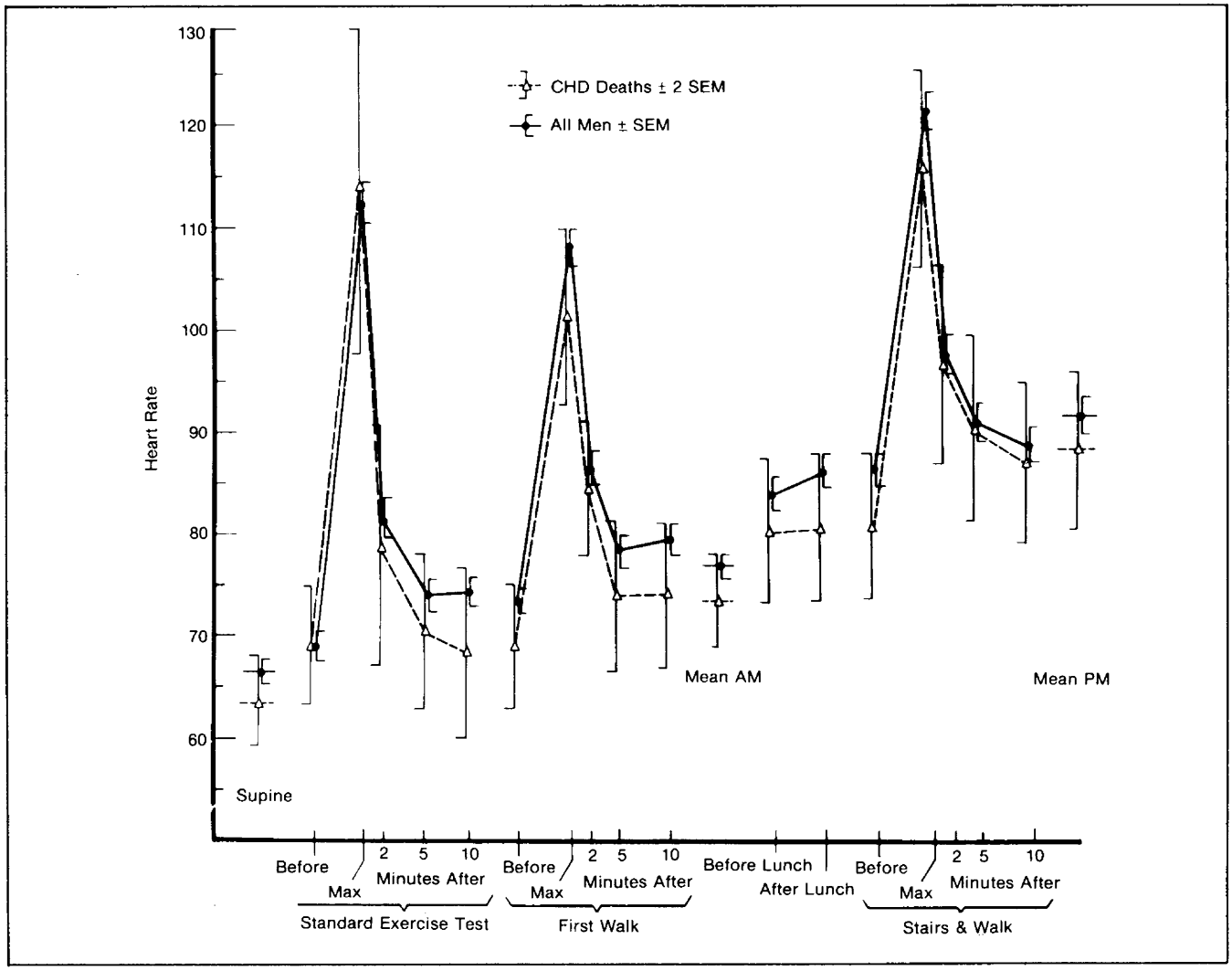


Fig 2.—The mean heart rates of the men whose deaths were attributed to coronary heart disease compared with the mean heart rates of all men in the sample.

than 70 beats per minute ($P < .005$); and (3) a maximum heart rate not greater than 99 beats per minute during the stair climb and walk immediately after lunch ($P < .005$). The 65 men who exhibited one or more of these phenomena at the time of their first recording accounted for ten of the 22 subsequent deaths for which rate data were available (5.1 deaths expected, $P < .01$). An additional death occurred in a man who did not exhibit one of these slow rate phenomena at the time of his first recording, but who did exhibit these at the time of his second recording which was obtained shortly before his death.

**"Sustained Relative Bradycardia."**—From these observed phenomena, an attempt was made to determine the "slow rate criterion" which would identify that group of men with slow heart rates who had the greatest proportion of acute cardiac deaths. By trial and error, the best criterion was found to be one based on: (1) a mean afternoon heart rate equal to or less than 70 beats per minute, or (2) a mean afternoon heart rate equal to or less than 80 beats per minute, provided the mean afternoon heart rate was not more than 15 beats per minute higher than the morning supine rate.

This criterion identified 34 men who accounted for eight of the subsequent coronary deaths (2.6 expected: $P < .002$). One other man who died a coronary death very nearly met this criterion also. The criterion identified, in addition, two men with coronary heart disease, one of whom died of a stroke and the other of whom died of bacterial endocarditis following a prostatectomy. Both of these men had definite hypertension. It identified one man with a probable coronary heart disease who died of

**Table 4.—Twenty-one Deaths Not Reported as Coronary Deaths: Prior Clinical Findings and Nature of Fatal Episode***

| Code No. | Preexisting Clinical Diseases | | | Sustained Relative Bradycardia | Clinical Characteristics of Fatal Episode |
|---|---|---|---|---|---|
| | Cardiac Heart | Hypertensive | Pulmonary | | |
| 88 | Probable MI CI, AP | Definite | — | SRB | HCV dis, stroke, resp failure |
| 100 | AP | Definite LVH | — | — | HVC dis, cerebral hemorrhage |
| 203 | ECG, MI, AP | Definite LVE | — | SRB | Bacterial endocarditis |
| 111 | — | Borderline | Ca of lung | — | Ca of lung |
| 142 | — | Definite | — | SRB | Carcinoma, inanition, cardiac failure |
| 236 | — | Definite | Emphysema | — | Ca of lung |
| 318 | — | — | OID, Emphysema | — | Ca of colon |
| 1 | — | Borderline | — | — | Ca of lung |
| 10 | — | — | Emphysema | SRB | Ca of lung |
| 50 | — | — | — | — | Ca of urinary bladder |
| 110 | — | — | Emphysema | SRB | Ca of lung |
| 145 | — | LVH | — | SRB | Ca of cecum |
| 172 | — | Definite | Bronchitis, emphysema | — | Emphysema, resp failure |
| 244 | — | — | — | — | Ca of colon and liver |
| 270 | — | Definite | — | — | Cirrhosis, hepatic failure |
| 291 | — | — | — | — | Retic cell sarcoma; hemorrhage |
| 306 | — | Borderline | — | — | Metastatic brain tumor |
| 316 | — | — | — | | Lymphatic leukemia, Ca of sigmoid; CHF |
| 347 | ISCH ST | Borderline | — | SRB | Ca of colon |
| 29 | — | — | — | — | Ca of urinary bladder |
| 200 | — | — | — | — | Ca of lung |

* MI = myocardial infarction, CI = coronary insufficiency, AP = angina pectoris, LVH = left ventricular hypertrophy, LVE = left ventricular enlargement on roentgenogram, HCV = hypertensive cardiovascular, Ca = cancer, OID = old inflammatory disease on roentgenogram, ISCH ST = ischemic ST segments and T-waves on standard ECG, and CHF = congestive heart failure.

Fig 3.—The mean heart rates of men with "sustained relative bradycardia" compared with those of all men in the sample.

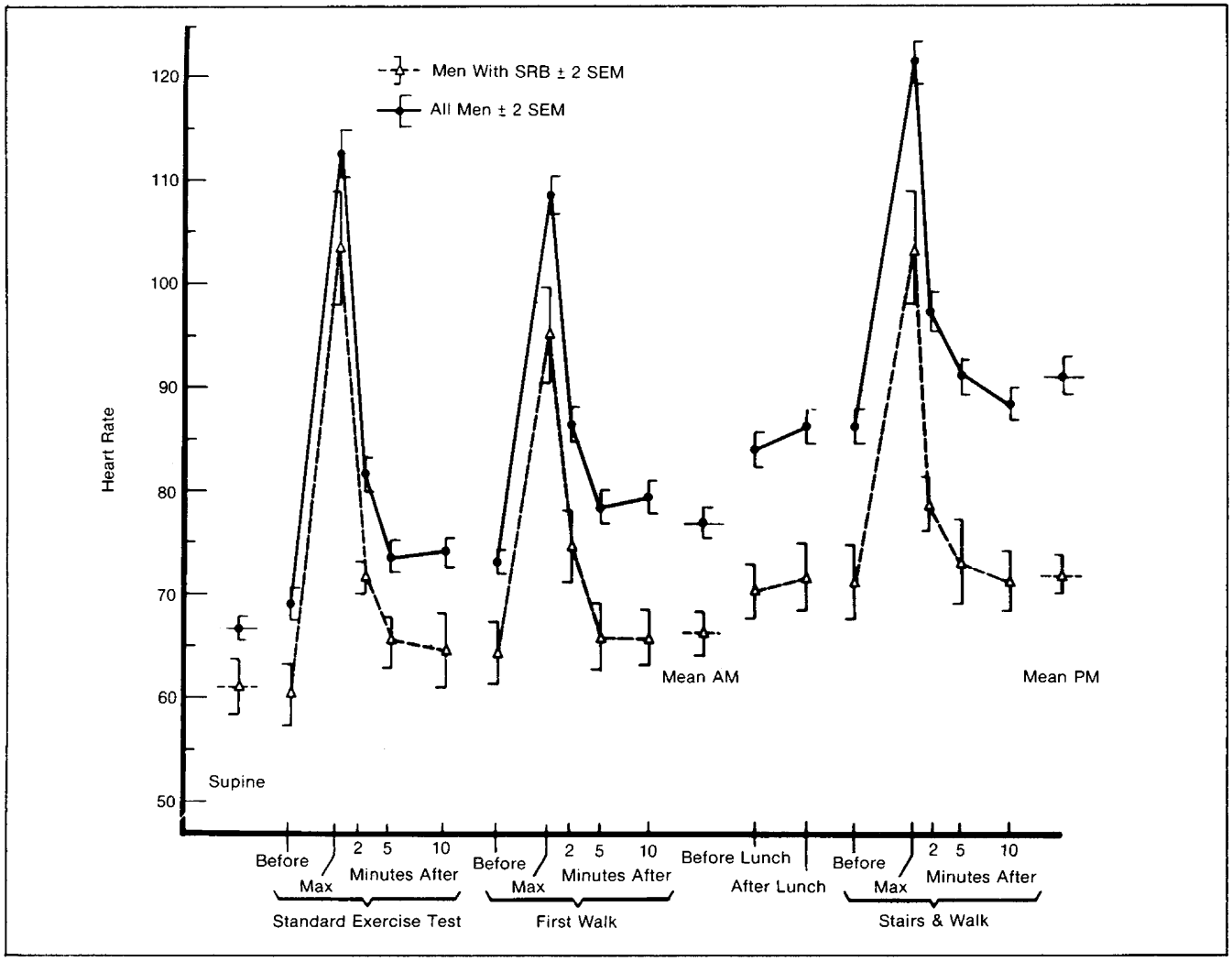

Table 5.—Thirty-Four Men With Sustained Relative Bradycardia: Findings at First Examination*

| Code No. | Preexisting Disease: Cardiovascular Heart | Preexisting Disease: Hypertensive | Preexisting Disease: Pulmonary | Heart Rates: AM Supine | Heart Rates: Mean PM | Heart Rates: PM-S | Heart Rates: Phas Var | Pacemaker: RASS | Pacemaker: P Axis | Pacemaker: PR Interval (sec) | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 65 | MI, AP | — | Bronchitis, emphysema | 67 | 75 | 8 | 9.7 | 0 | +60° | 0.16 | |
| 138† | MI, CI, AP | Definite | — | 71 | 74 | 3 | ND | 0.14 | +30° | 0.12 | WAP |
| 157† | MI, AP | — | — | 62 | 76 | 14 | 17.6 | 0.14 | +45° | 0.14 | |
| 88 | CI, AP | Definite | — | 66 | 70 | 4 | 14.6 | 0 | +60° | 0.14 | |
| 89† | CI, AP | — | Emphysema | 65 | 77 | 12 | 10.8 | 0 | +75° | 0.18 | |
| 118 | AP | Definite | — | 48 | 70 | 22 | 11.3 | 0 | +30° | 0.12 | |
| 187 | AP | — | — | 50 | 64 | 14 | ND | ND | +75° | 0.18 | WAP |
| 230 | Probable MI | Definite | — | 58 | 62 | 9 | ND | 26.8 | +60° | 0.14 | |
| 336 | CI, AP | — | — | 75 | 80 | 5 | 13.8 | 0 | +15° | 0.16 | |
| 115† | ISCH ST | Definite LVH | — | 59 | 57 | −2 | ND | 0 | +60° | 0.16 | |
| 135† | ISCH ST | Definite LVH | — | 55 | 68 | 13 | 14.7 | 0 | +60° | 0.14 | |
| 203 | — | — | — | 66 | 77 | 11 | ND | ND | +60° | 0.16 | |
| 142 | — | — | — | 66 | 80 | 14 | 10.5 | 0 | +60° | 0.14 | |
| 195 | — | Definite | Asthma | 56 | 68 | 12 | ND | 0 | +15° | 0.16 | |
| 269 | — | Definite | Emphysema | 71 | 75 | 4 | 13.2 | 0.14 | +60° | 0.16 | |
| 3 | — | Definite | — | 64 | 79 | 15 | 10.6 | 1.7 | +75° | 0.18 | |
| 10 | — | — | Emphysema | 68 | 76 | 8 | ND | 0.60 | +60° | 0.18 | WAP |
| 12 | — | — | OID | 63 | 77 | 14 | 14.4 | 0.25 | −45° | 0.16 | |
| 28† | — | — | — | 61 | 72 | 11 | 11.6 | 0 | +60° | 0.16 | |
| 71 | — | — | — | 61 | 69 | 8 | 9.9 | 0 | +30° | 0.14 | WAP |
| 74 | — | — | — | 63 | 78 | 15 | ND | 0 | +60° | 0.16 | |
| 75 | — | — | — | 60 | 73 | 13 | 11.4 | 0.33 | +60° | 0.16 | |
| 101† | — | Definite LVH | — | ND | 62 | ND | ND | 0 | +60° | 0.14 | WAP |
| 110 | — | — | Emphysema | 65 | 72 | 7 | 9.92 | 0 | +75° | 0.14 | WAP |
| 145 | — | Definite LVH | — | 58 | 67 | 9 | ND | 0 | +60° | 0.14 | |
| 158 | — | — | — | 66 | 80 | 14 | 12.8 | 0 | +90° | 0.20 | |
| 275† | — | — | Bronchitis, emphysema | 47 | 64 | 17 | ND | 0 | −105° | 0.10 | AVNR |
| 283 | — | — | — | 43 | 67 | 24 | 8.37 | 0.17 | +75° | 0.16 | |
| 295 | — | — | — | 61 | 72 | 11 | 16.9 | 4.67 | +60° | 0.14 | |
| 345 | — | — | — | 53 | 70 | 17 | ND | 3.33 | +45° | 0.14 | |
| 347 | — | — | — | 65 | 79 | 14 | 13.8 | 6.75 | +45° | 0.14 | |
| 188 | — | — | — | 62 | 75 | 13 | 18.6 | 0.43 | +60° | 0.18 | |
| 207 | — | — | — | ND | 70 | ND | 13.2 | 0.17 | +60° | 0.18 | |
| 254 | — | — | — | 57 | 69 | 12 | 15.3 | 0.71 | +60° | 0.14 | |

* PM-S = difference between mean afternoon heart rate and morning supine heart rate, rate per minute; Phas Var = phasic variation in heart rate, measured as mean maximum magnitude of variation in rate per minute; RASS = random abrupt sinus slowing, expressed as episodes per hour; P Axis = frontal plane axis of P vector, in degrees; SPC = supraventricular premature contraction; VPC = ventricular premature contraction; MI = myocardial infarction; AP = angina pectoris; CI = coronary insufficiency; Trans IVCD = transient intraventricular conduction disorder; ND = no data; WAP = wandering atrial pacemaker; 2F = two foci; 0.11 QRS time, 0.11 seconds; ISCH ST = ischemic ST patterns and T waves on standard ECG; IVB = intraventricular block; AVB = atrioventricular block; BBB = bundle branch block; BI = bigeminy; OID = old inflammatory disease on roentgenogram; MSPC = multiple consecutive supraventricular premature contraction; RVCD = right ventricular conduction defect; AVNR = atrioventricular nodal rhythm; Prs = paired premature contractions; definite (Def) = blood pressure ≧160/95 mm Hg, and borderline (Bord) = blood pressure ≥140 to 159/90 to 94 mm Hg.

† Subsequent coronary deaths.

carcinoma of the colon. It identified two men with hypertension, one of whom died of cardiac failure with advanced carcinoma of the prostate and another of whom died of carcinoma of the cecum; and it identified two men with emphysema who died of carcinoma of the lung.

As a group, these 34 men who had slow heart rates and a high risk of subsequent acute cardiac death exhibited the following characteristics of their heart rate during the six-hour observation (Fig 3):

1. Their morning supine rates were slow. The mean for all men who showed one or more of the slow rate phenomena was 59.1 ± 1.9. The mean supine rate for the 34 men who met the slow rate criterion was 61.0 ± 2.6.

2. Their heart rates did not rise

| Dysrhythmias | | |
|---|---|---|
| SPCs per 1,000 | VPCs per 1,000 | Conduction |
| 0 | 0 | Trans IVCD |
| 0 | 2.1 2F | 0.11 QRS; preexcitation pattern |
| 0.4 | 0.5 | Trans IVCD |
| 0.3 | 0.7 | Trans 0.11 QRS; IVB |
| 0.4 | 0.4 3F | |
| 0.1 | 0.5 2F | −30° QRS axis |
| 0.1 | 0.1 | |
| 0.1 | 0.8 2F | Ind QRS axis |
| 0.4 | 0.3 | Trans 0.11 QRS: IVB |
| 0 | 3.0 | 2:1 AVB; 0.10-0.16 QRS; bilateral BBB |
| 0.4 | 0.1 | 0.10 QRS |
| 0 | 4.5 Bl | |
| 0.1 | 1.7 2F | |
| 0.4 | 0 | |
| 0.1 | 19.8 2F | Ind QRS Axis |
| 0 | 0.1 | |
| 0.2 | 0.1 | |
| 36.2 Tri | 0.1 | |
| 0.1 MSPC | 0 | Trans 0.10 QRS |
| 0.1 | 0 | −60° QRS axis |
| 0.3 | 0 | |
| 0.5 | 1.1 2F PVT | Trans 0.11 QRS IVB; −30° axis |
| 0.1 | 0.6 | Trans 0.11 QRS IVB |
| 26.2 | 0 | |
| 0.4 | 0 | 0.10 QRS RVCD |
| 3.9 | 0.1 | |
| 44.3 Prs Bl MSPC | 13.54 Bl Prs | 0.10 QRS: −45° axis |
| 0.1 | 25.2 Prs | $S_1$ $S_2$ $S_3$ |
| 2.7 | 2.3 | |
| 1.4 | 1.8 2F | Trans 0.10 QRS |
| 0.1 Prs | 0 | |
| 0 | 0.1 | |
| 0.4 | 0 | |
| 0.1 | 1.8 2F | RVCD |

significantly during the day. The failure of the heart rate to rise during the course of the day's activity appeared to be more significant than the supine rate itself. There were 191 men with supine rates of 70 beats per minute or less. Among these 191 men there were 31 men whose heart rate did not rise more than 15 beats per minute from the supine rate to the mean afternoon rate. These men experienced six subsequent acute cardiac deaths (2.4 expected; $P < .02$). Among the remaining 160 men with supine rates of 70 or less whose mean afternoon rates were more than 15 beats per minute higher than their supine rates, there were ten subsequent coronary deaths (12.4 expected, NS).

3. During six hours of light activity, including a large meal, the heart rates of these men were significantly lower than the heart rates of other men in the sample, and their mean heart rates in the afternoon after the large meal were strikingly lower. The mean afternoon heart rate of the 34 men who met the slow rate criterion was 72.0 ± 1.9.

We have referred to the phenomenon of persistent slow heart rate with a low peak rate response to exercise as "sustained relative bradycardia" (SRB). For investigational purposes we have defined sustained relative bradycardia by the arbitrary slow rate criterion described in the paragraphs above.

The eight men who had SRB at the time of their first examination and who subsequently died coronary deaths included four men who had overt and two who had probable coronary heart disease, of whom four had definite hypertension also, three had LVH pattern on their ECGs, and one had emphysema. The group also included one man who had definite hypertension and LVH pattern, but who had no clinical evidence of coronary heart disease; one man with emphysema and bronchitis but no clinical evidence of coronary heart disease; and one man who had no clear-cut evidence of any of these conditions, although he did have diabetes. Three of these men were smoking two packs or more of cigarettes each day at the time of their death.

**Sustained Relative Bradycardia and Preexisting Cardiac and Pulmonary Disease.**—Sustained relative bradycardia was slightly more frequent among men with preexisting "definite" and "probable" coronary heart disease than among men without coronary heart disease (Table 5). Of the 34 men with sustained relative bradycardia, three had previous clinical myocardial infarctions, five had previous episodes of angina pectoris or coronary insufficiency, and one had preexisting electrocardiographic evidence of prior myocardial infarction, without a clinical history of myocardial infarction. Of the 25 men with sustained relative bradycardia who did not have such definite evidence of coronary heart disease, two had "nonspecific" ST- and T-wave abnormalities on their ECGs and one had pain rated as probable angina pectoris by the examining physician who saw him. Altogether, 12 of the 34 men with sustained relative bradycardia had definite or probable coronary heart disease (6.7 expected, $P < .02$).

Eleven men with SRB had blood pressures of 160/95 mm Hg or higher (11 expected, NS). Five had LVH patterns on their standard electrocardiograms (2.5 expected, $.1 > P > .05$). Seven men with SRB had bronchitis, emphysema, or asthma (8.2 expected, NS). Twenty-five men with SRB had smoked for 30 years or more (25.0 expected, NS). Four men were now smoking two packs of cigarettes or more per day (3.1 expected, NS).

Sustained relative bradycardia was not more frequent than expected among men with obesity, diabetes mellitus, cholesterol levels above 300 mg/100 ml, or serum uric acid levels above 7.0 mg/100 ml. Men with SRB did not include more than the expected number of men who were taking cardiac or antihypertensive medications or other medications that might affect the heart rate. Men with SRB were neither more active nor less active than other men in the sample. Their mean daily caloric expenditure in all activities was 2,898 ± 94.6 kilogram calories.

**Sustained Relative Bradycardia and Disorders of the Cardiac Pacemaker.**—The frequency of asymptomatic

**Table 6.—Thirty-Four Men With Sustained Bradycardia Findings at Second Examination***

| Code No. | Events in Interval | Found at Examination: Cardiovascular Heart | Hypertensive | Pulmonary | Heart Rates: AM Supine | Mean PM | PM-S | Pacemaker: P-Axis | PR Int | |
|---|---|---|---|---|---|---|---|---|---|---|
| 65 | AP | MI AP | — | Bronchitis, emphysema | 62 | 73 | 11 | +60° | 0.16 | |
| 138† | MI death | — | — | — | — | — | — | — | — | |
| 157† | Abrupt death | — | — | — | — | — | — | — | — | |
| 88 | Probable MI, CHF, AP | Probable MI CI AP | Definite | — | 72 | 87 | 15 | +60° | 0.14 | |
| 89† | AP ECG MI CHF | ECG CI AP | Definite LVE | Emphysema | 66 | 80 | 14 | +30° | 0.17 | |
| 118 | AP | AP | Definite | — | 46 | 70 | 24 | +30° | 0.14 | |
| 187 | Atypical angina | AP | Definite | ? | ND | ND | ND | +75° | 0.16 (ND on WAP) | |
| 230 | AP | Probable MI AP | Definite | — | 70 | 84 | 14 | +25° | 0.12 WAP, AVNR | |
| 336 | — | CI AP | — | — | 83 | 69 | −14 | +30° | 0.16 | |
| 115† | — | ISCH ST | Definite | — | 52 | 56 | 4 | +60° | 0.20 | |
| 135† | MI death | — | — | — | — | — | — | — | — | |
| 203 | ECG MI | Probable ECG AP | Definite LVE | | 101 | 85 | −16 | +60° | 0.18 | |
| 142 | — | — | Definite | . . . | 75 | 95 | 20 | +30° | 0.14 | |
| 145 | — | — | Definite | Asthma | 56 | 64 | 8 | +30° | 0.16 | |
| 269 | — | — | Definite | Emphysema | ND | ND | ND | +60° | 0.18 | |
| 3 | Stroke-CHF | ISCH ST | Definite | — | 65 | 72 | 7 | +60° | 0.20 | |
| 10 | Ca of lung—death | — | — | — | — | — | — | — | — | |
| 12 | — | — | — | OID | 68 | 87 | 19 | Varies | Varies WAP | |
| 28† | ECG MI | ECG | LVE | . . . | 64 | 70 | 6 | +30° | 0.19 | |
| 71 | — | — | Definite LVE | . . . | 62 | 71 | 9 | +30° | 0.18 WAP | |
| 74 | — | — | — | OID | 59 | 75 | 16 | +60° | 0.20 | |
| 75 | — | — | — | — | 50 | 66 | 16 | +30° | 0.20 | |
| 101† | Abrupt death | — | — | — | — | — | — | — | — | |
| 110 | Ca of lung—death | — | — | — | — | — | — | — | — | |
| 145 | — | ISCH ST | Definite LVH | — | 51 | 70 | 19 | +60° | 0.18 | |
| 158 | Arrhythmia | — | — | — | 60 | 75 | 15 | +60° | 0.22 | |
| 275† | CHF | — | LVE | Bronchitis, emphysema | 86 | 105 | 19 | — | — AF | |
| 283 | Syncope × 3 | — | — | — | 52 | 75 | 18 | +75° | 0.18 | |
| 295 | — | — | — | — | 57 | 67 | 10 | +60° | 0.14 | |
| 345 | Arrhythmia | — | — | — | 65 | 75 | 10 | +60° | 0.18 | |
| 347 | — | ISCH ST | — | — | 59 | 70 | 11 | +60° | 0.16 | |
| 188 | — | — | — | — | 66 | 75 | 9 | +45° | 0.20 | |
| 207 | — | — | — | — | 60 | 60 | 0 | +60° | 0.18 | |
| 254 | — | — | Definite | OID | 88 | 104 | 16 | +60° | 0.18 | |

* Ca = cancer, CHF = congestive heart failure; for remaining definitions see Tables 4 and 5.
† Coronary deaths.

dysrhythmias and the frequency of disorders of the cardiac pacemaker and conduction system among men in this sample have been described in other publications.[1,12]

*Definite Disorders of the Pacemaker.*—Thirty-six of the 301 had primary cardiac pacemakers which were not in a normal location in the sinoatrial (SA) node. The evidence for this was (1) a PR interval equal to or less than 0.12 seconds; (2) a frontal plane P-axis of 0°, or negative; or (3) the presence of a wandering atrial pacemaker or an A-V junctional rhythm. These 36 men experienced seven subsequent coronary deaths (2.8 expected, $P < .01$). Three other men had periods of SA block.

*Possible Disorders of the Pacemaker.*—There were eight men who had primary pacemakers that appeared to be normally located in the SA node, but which may not have been functioning in an entirely normal manner. The evidences for this were the following:

1. There was marked diminution of the amplitude of the phasic variations of the heart rate with respiration. These phasic variations, which appear to be universally present in young people with healthy hearts, were much diminished or absent in some members of the sample.[12] At a heart rate of 80 beats per minute, the frequency of these variations among the men in this sample ranged from 6 to 20 cycles per minute and the maximum magnitude of the variations in any one minute ranged from 7.57 to 25.59 beats per minute. There were 15 men in the sample who displayed minimal to absent phasic variations in heart rate as defined by a max-

| Dysrhythmias | | |
|---|---|---|
| APCs per 1,000 | VPCs per 1,000 | Conduction |
| 0 | 0 | Trans IVCD ? |
| — | — | |
| — | — | |
| 0 | 21 | Trans IVB |
| <1 | 1-9.9 | 0.10 QRS |
| 0 | <1 | −30° QRS |
| ND | ND | |
| ND | ND | IVB QRS axis |
| 0 | 1-9.9 | Trans 0.11 QRS IVB |
| 0 | 1-9.9 | 2:1 AVB 0.14 QRS, right BBB |
| — | — | — |
| 0 | 1-9.9 | −30° QRS axis |
| 0 | <1 | |
| 0 | <1 | |
| ND | ND | +75° QRS axis |
| 0 | 1-9.9 | |
| — | — | — |
| >10 | >10 | QRS axis 60° left to 0 |
| 1-9.9 | >10 | 0.10 QRS; ind axis |
| 0 | 0 | −45° QRS axis |
| 0 | 0 | Ind QRS axis |
| 0 | 1-9.9 | 0.10 QRS −30° axis |
| — | — | — |
| — | — | — |
| 0 | 1-9.9 | 0.10 QRS, RVCD |
| 0 | 0 | 1 AVB |
| — | >10 | 0.10 QRS −45° axis |
| 0 | >10 | $S_1$ $S_2$ $S_3$ |
| 1-9.9 | >10 | — |
| >10 | 1-9.9 | Trans 0.10 QRS: +75° axis |
| 0 | <1 | |
| 0 | <1 | |
| 0 | 0 | |
| <1 | <1 | |

imum mean phasic variation of less than 10 beats per minute.

2. There was an absence of random episodes of abrupt sinus slowing. This phenomenon, which is quite striking in young people, is readily produced by sighing, yawning, coughing, or straining. In our experience it has occurred at a frequency of one or two episodes per hour in most records of healthy young people.[12] It occurred at this frequency among many of the men in our sample; however, there were 92 men in the sample who did not exhibit this phenomenon. Absence of this phenomenon was significantly associated with evident abnormalities of the pacemaker; but 69 men in the sample showed only this abnormality.

These two phenomena were considered to be evidence of a possible disorder of the pacemaker, because they increased in frequency with increasing age, because they were often associated with or followed by the development of definite abnormalities of the pacemaker, and because the absence of episodes of sinus slowing in our sample was associated with the presence of coronary heart disease (18 cases observed, 11.6 expected, $P < .02$) and was followed by more than the expected number of episodes of subsequent acute cardiac death (13 deaths observed, 8.9 expected, $P < .005$).[12]

At the first examination, four men with SRB had minimal evidence of phasic variation (mean maximum amplitude of variation in any one minute less than 10 beats per minute) (Table 5). Six others had significantly diminished phasic variations as compared to other men in the sample (mean maximum magnitude of phasic variation less than 11.5 beats per minute). The mean maximum magnitude of phasic variation for all men with sustained relative bradycardia was 12.64 ± 1.08 beats per minute. This was significantly less than the mean maximum magnitude for all other men in the sample ($P < .01$) (one-tail $t$ test).

Seventeen of the men with SRB had no episodes of sinus slowing (10.1 expected, $P < .01$); six others had only one episode in six hours.

Three men with SRB had PR intervals of 0.12 second or less. Thirteen others had PR intervals of 0.12 to 0.14 second (9.5 expected, $P = .01$).

The mean PR interval for men with SRB was 0.1529 ± 0.0059 seconds. The mean PR interval for all men was 0.1622 ± 0.0026 second ($P < .01$) (one-tailed $t$-test).

Two men with SRB had frontal plane P-axis of −45° and −105°, respectively. Six had wandering atrial pacemakers; one had a slow A-V junctional rhythm.

Altogether, 9 of the 34 men with SRB had abnormally located pacemakers and 12 had possible abnormalities of pacemaker function ($P < .01$). There was only one man among the 34 who had phasic variations of larger than average magnitude, sinus slowing of average frequency and a normally located pacemaker.

**Sustained Relative Bradycardia and Disorders of Cardiac Conduction.**—At the first examination, ten of the 34 men with SRB had definite disorders of cardiac conduction (8.0 expected, NS) and nine others had abnormalities considered to represent possible disorders of conduction.

One man had a consistently prolonged QRS interval of 0.11 seconds with a pattern consistent with preexcitation. One man had a QRS interval which varied from 0.10 to 0.16 seconds with a pattern of right bundle branch block (RBBB) and left bundle branch block (LBBB) alternating with type II 2:1 A-V block; this probably represented alternating bundle conduction and trifascicular block. Four men who had normal QRS conduction on their standard ECGs had transient periods of prolonged QRS conduction ( ≥ 0.11 second) and an abnormal pattern in their taped records. Three men had abnormal QRS patterns without prolonged conduction: two men had regular sinus rhythm (RSR) patterns in $V_1$ and one man had an $S_1$ $S_2$ $S_3$. One man with frontal plane QRS axis of −60° was considered to have a left anterior hemiblock.

The men with possible abnormalities of QRS conduction included one man with a QRS interval of 0.10 second and a frontal plane QRS axis of −45°, one man with a constant QRS interval of 0.10 second, two men with QRS intervals transiently of 0.10 second, two men with transient abnormal QRS patterns without prolongation of the conduction time, one man with a QRS axis of −30°, and two who had indeterminate QRS axes.

Table 7.—Thirty-Four Men With Sustained Relative Bradycardia—Six-Year Follow-up*

| Code No. | Present Status | Disease Present at Last Examination | Pacemaker and Conduction at Last Examination |
|---|---|---|---|
| 65 | Living | CH Dis (MI, AP), bronchitis, emphysema | PV 9.7, RASS 0, Trans IVCD |
| 138 | Died abruptly 3 hr after onset of acute MI | CH Dis (MI, CI, AP), Hyp Def | PR 0.12, WAP 0.11 QRS preexcitation pattern |
| 157 | Died abruptly and unexpectedly | CH Dis (MI, AP) | RASS 0.14, PR 0.14 Trans IVCD |
| 88 | Died—Stroke | CH Dis (probable MI, CI, AP), Hyp Def, CHF | RASS 0, PR 0.14, Trans IVCD |
| 89 | Died abruptly after 4 days of CHF | CH Dis (ECG, MI, CI, AP), Hyp Def LVH, emphysema | PV 10.9, RASS 0, 0.10 QRS |
| 118 | Living | CH Dis (AP) Hyp Def | PV 11.3, RASS 0, PR 0.14, −30° QRS axis |
| 187 | Living | CH Dis (AP), Hyp Def | WAP |
| 230 | Living | CH Dis (MI, AP), Hyp Def | WAP AVNR PR 0.12, Ind QRS axis |
| 336 | Living | CH Dis (CI, AP) | RASS 0, Trans 0.11, QRS IVB |
| 115 | Died abruptly and unexpectedly | CH Dis (ISCH ST), Hyp Def, LVH | RASS 0, 2:1 AVB (Mobitz II) 0.14 QRS RBBB |
| 135 | Died in shock 1 hr after onset of acute MI | Hyp Def, LVH | RASS 0, PR 0.14, 0.10 QRS |
| 203 | Died of acute bacterial Endocarditis | CH Dis (ECG, MI, AP), Hyp Def, LVE | −30° QRS axis |
| 142 | Died—cancer of prostate, inanition, CHF | Hyp Def | PV 10.5, RASS 0, PR 0.14 |
| 195 | Living | Hyp Def, Asthma | RASS 0 |
| 269 | Living | Hyp Def, emphysema | RASS 0.14, VPCs 19.8/1000, +75° QRS axis |
| 3 | Living | Stroke, CHF Hyp Def, ISCH ST | PV 10.6 PR 0.20 |
| 10 | Died—cancer of lung | Emphysema | WAP |
| 12 | Living | OID lung | WAP 10 VPCs per 1,000 |
| 28 | Died abruptly and unexpectedly | CH Dis (ECG, MI), LVE | PV 11.6, RASS 0, 0.10 QRS Ind axis 10 VPCs per 1,000 |
| 71 | Living | Hyp Def, LVE | PV 9.7, RASS 0, WAP −45° QRS axis |
| 74 | Living | OID lung | RASS 0, Ind QRS axis |
| 75 | Living | — | PV 11.4, 10 QRS, −30° axis PVT |
| 101 | Died abruptly and unexpectedly | Hyp Def, LVH | RASS 0, WAP, Trans 0.11 QRS IVB |
| 110 | Died—cancer of lung | Emphysema | PV 9.9, RASS 0, WAP |
| 145 | Died—cancer of cecum | CH Dis (ISCH ST), Hyp Def, LVH | RASS 0, 0.10 QRS RVCD |
| 158 | Living | Arrhythmia | PR 0.22 |
| 275 | Died abruptly and unexpectedly | Bronchitis, emphysema, LVE, CHF | AF 0.10 QRS −45° axis 10 VPCs per 1,000 |
| 283 | Living | Syncope × 3 | $S_1$ $S_2$ $S_3$, 10 VPCs per 1,000 |
| 295 | Living | Hyp Bord | PR 0.14, 10 SPCs per 1,000 |
| 345 | Living | Arrhythmia | PR 0.14, 10 SPCs per 1,000 Trans 0.10 QRS, +75° axis |
| 347 | Died—cancer of colon | CH Dis (ISCH ST) | PR 0.14 |
| 188 | Living | — | PR 0.20 |
| 207 | Living | — | — |
| 254 | Living | Hyp Def, OID, lung | PR 0.14, 0.10 QRS RVCD |

* CH Dis = cardiovascular heart disease; Hyp = hypertensive disease; PR = PR interval, in seconds. For remaining definitions, see Table 5.

**The Subsequent Course of Men With Sustained Relative Bradycardia.**—In the interval between the first and second examination, six of the men with SRB died. One man who had coronary heart disease, and one who had hypertension and an LVH pattern on his electrocardiogram, died abruptly. Another man who had coronary heart disease and another who had hypertension and LVH developed myocardial infarctions and died. Two men, both of whom had bronchitis and emphysema, died of carcinoma of the lung.

Twenty-eight men survived until the second examination, and 26 were examined completely. Two men who could not be reexamined were contacted by telephone, were seen by their private physicians, and submitted to new electrocardiograms. One of these, who had previously had angina pectoris and hypertension, had experienced probable myocardial infarction in the interval; the other had emphysema and said he was unable to come to New York.

Nineteen of the 26 men who were reexamined in 1967 to 1969 again had

sustained slow heart rates (Table 6). Sixteen of these men met the original criteria for sustained relative bradycardia; two others almost did so. Two men who formerly had sustained relative bradycardia now had developed sustained tachycardia. One of these men had developed a rapid atrial fibrillation.

Five of the survivors still had PR intervals of 0.14 seconds or less; but there were four men whose PR intervals had lengthened to 0.20 seconds, and one man had developed a PR interval of 0.22 seconds. Four of the six men who originally had wandering atrial pacemakers had died, and one had become disabled; but an additional man had developed a wandering atrial pacemaker and had large numbers of atrial and ventricular dysrhythmias. Another man now had periods of A-V junctional rhythm. The man who originally had a slow A-V junctional rhythm now had rapid atrial fibrillation.

In addition to the five men who had prolonged their A-V conduction, there were two men who shifted their QRS axes leftward by 60°, two others who had shifted QRS axes rightward to 75°, and one who had developed an indeterminate QRS axis. One man developed an LVH pattern with QRS interval of 0.10 seconds.

At the time of the original examination, three men with SRB had 10 or more ventricular premature contractions (VPCs)/1,000 complexes, and three men had ten or more atrial premature contractions (APCs)/1,000 complexes (one man had both). At the second examination, two additional men had more than 10 VPCs/1,000 complexes.

In the interval between the two examinations, three men with SRB developed electrocardiographic evidence of previous myocardial infarctions (QRS criteria). One man developed angina pectoris; two men with hypertension developed left ventricular enlargement on the roentgenogram. Two men, formerly with uncomplicated SRB, were treated in the interval by their private physicians for "acute arrhythmias"; the nature of the arrhythmias was not documented. Another man had three unexplained and unexpected episodes of syncope. Three men with SRB went into congestive heart failure.

After the examination, three men with SRB died abrupt cardiac deaths. Two of these were men with electrocardiographic evidence of previous myocardial infarction; the third was a man with rapid atrial fibrillation. Two other men died of carcinoma of the cecum and colon, and one man, who had had hypertension and LVE, died of a gram-negative endocarditis which developed after a prostatectomy.

Seven years after the initial examination, 15 of the 34 men with SRB were dead (5.0 expected, $P < .001$). Five had died abruptly and unexpectedly (1.7 expected, $P < .01$) (Table 7). Two had died within three hours after the onset of an acute myocardial infarction. Three had died in congestive heart failure, including one who had carcinoma of the prostate. One man had died of endocarditis, and four had died of cancer (Table 7).

Five of the 19 survivors had overt coronary heart disease. Six had definite hypertension, including three who also had coronary heart disease, and two who had pulmonary disease. Two men had bronchitis and emphysema, one had asthma, and one had old pulmonary inflammatory disease (two of these had hypertension also, and one had coronary heart disease). Two men, not included in those above, had had clinically significant episodes of dysrhythmia, and one man had had recurrent unexplained episodes of syncope. Twenty-one of the men with SRB had (or had died with) evidence of disease of the cardiac pacemaker. Twenty-three of the men had (or had died with) evidence of disorders of cardiac conduction. Five had no definite or probable disorder of either the pacemaker or the conduction system, but two of these had significantly prolonged their PR intervals during the past five years, one had developed large numbers of ventricular dysrhymias, and one had developed ischemic ST segments on his standard ECG. Only one man survived with SRB, who had no evidence of coronary heart disease, hypertension, or pulmonary disease, and no apparent abnormalities of his pacemaker or conduction system.

## Comment

Although sinus bradycardia is an occasional manifestation of a number of diseases,[13,14] a sustained slow heart rate is such a well-known concomitant of physical fitness in young men and athletes[15] that it has become a medical rule of thumb that a slow heart rate in the absence of obvious disease is an indication of a relatively healthy and fit man. However, it was not so in this random sample of middle-aged American men. Here, some sustained slow heart rates were an indication of ill health and of poor physical condition, and the men who had these slow heart rates had a much higher subsequent death rate than other men in the sample.

The 34 men in the sample who exhibited sustained relative bradycardia, as we have defined it, were not young men. They were not healthy men, and they were not athletes. They were men between the ages of 55 and 60 years. Although they were actively employed and not disabled at the time that we first saw them, the majority of them had coronary heart disease, hypertension, pulmonary disease, or some combination of these three conditions. Many of them were obese, many of them had elevated blood lipid levels, most of them had smoked for more than 30 years, and all of them led essentially sedentary lives. None of them took any active physical exercise other than walking, golfing, or gardening. The largest daily mean caloric expenditure of any man in the group was 3,554 kilogram calories. Twenty-nine of the 34 expended less than 3,000 kilogram calories per day. Many of them had overt disorders of their cardiac pacemakers at the time that we first examined them. Many who did not have such

disorders developed them before their second examination.

The slow heart rates that were associated with subsequent high death rates were of a special kind. Men who had a sinus bradycardia when they lay supine in the morning or when their standard electrocardiograms were being taken did not necessarily exhibit the sustained relative bradycardia that seemed to be the precursor of subsequent death. The heart rate of a man with SRB might be only relatively slow at such a time—between 60 and 70 beats per minute, rather than below 60 beats per minute. Men with SRB were not men who often developed a pronounced sinus bradycardia in response to vagal stimuli. They usually exhibited little or none of the spontaneous sinus slowing that occurs in most people's records when they cough, sneeze, sigh, or yawn. Men with SRB were men who had an initially slow or relatively slow heart rate which did not speed up greatly during the course of the day. Their hearts responded to modest levels of exercise; but since they started at a slower rate, their peak rate response during exercise was lower than that of the hearts of other men in the sample. After the exercise ended, their hearts returned to their slow intrinsic rate.

The hearts of men with sustained relative bradycardia behaved as if they were being driven by cardiac pacemakers which were intrinsically slower than the normal cardiac pacemaker and less responsive to neural influences. Sinus bradycardia is known to occur frequently in association with overt disease of the sinus node.[16] There was a good deal of evidence to support the conjecture that the normal pacemaker in the SA node of some of these men had been damaged or rendered inactive, and had been replaced by another pacemaker with an intrinsically slower rhythm.

Many of the men with SRB had shorter than normal PR intervals, as one might expect if their cardiac pacemakers were located in the coronary sinus or nearer to the AV junction, or if the impulse from the pacemaker was conducted by an abnormal pathway. The P wave of some of them had an abnormal axis in the frontal plane, also suggesting that there was an AV junctional location of the pacemaker, or different pathways of atrial activation, or both. A number of them had wandering atrial pacemakers with indications that several pacemakers in the atrium were alternately driving the heart. One man had an AV junctional rhythm, and another developed such a rhythm during the course of the observation period. With the passage of time, more and more of the men with SRB showed evidence of disorders of the cardiac pacemakers. In some instances the sustained relative bradycardia appeared to be the first evidence that such a disorder of the pacemaker was developing.

Many of the men with SRB also had disorders of the cardiac conduction system. One man had a 2:1 AV block which did not, however, account for his slow heart rate throughout the day, since it appeared only during periods of activity when his intrinsically slow sinus rate rose in the mid-seventies. The disorders of cardiac conduction, like the disorders of the pacemaker, increased in frequency and severity with the passage of time. At the second examination four men were found to have lengthened their PR intervals to the upper limit of normal and one had developed a PR interval of 0.22 seconds. Ten others had developed evidence of new disorders of QRS conduction which they had not exhibited before. Nevertheless, the conduction disturbances did not appear to account for the slow heart rates. The presence of conduction defects among men in the sample was only weakly associated with the presence of sustained relative bradycardia, but the presence of disorders of the pacemaker was strongly associated with the presence of this phenomenon.

Sustained relative bradycardia was a highly significant antecedent of cardiac death. The 34 men with SRB accounted for eight of the 26 subsequent deaths that were reported as coronary deaths, and two other coronary deaths occurred in men who had essentially slow heart rates that very nearly met the criteria for SRB. The 34 men with SRB accounted for five of the 14 sudden and unexpected deaths, and they also accounted for three of the men who died abruptly in the course of acute congestive heart failure or acute myocardial infarction. Sustained relative bradycardia appeared to be a significant antecedent of abrupt dysrhythmic death, whether this death occurred in the setting of acute myocardial infarction or an episode of congestive heart failure, or whether it appeared simply as a sudden and unexpected death of a man who had not previously seemed to be acutely ill.

The risk of death associated with the presence of SRB is not accounted for by the concomitant occurrence of large numbers of VPCs. Sustained relative bradycardia and frequent ventricular dysrhythmias appear to be indications of independent risk factors that are not associated with each other more often than chance would dictate. Only three of the 34 men with SRB had more than 10 VPCs/1,000 complexes at the first examination (3.0 expected, NS). Only one of the six men with many VPCs who died also had SRB. Large numbers of VPCs were more often associated with rapid heart rates than with slower heart rates. It is our present belief that large numbers of VPCs may be an indication of the presence of an area of relative ischemia in the ventricle, while sustained relative bradycardia may be an indication of disease of the cardiac pacemaker.

Although all of the abrupt deaths that occurred among the men in this sample were regarded as coronary deaths by the physicians who were in attendance at the time of the deaths, the clinical data prior to the time of the death did not necessarily indicate that coronary heart disease was present. This was true also of the men who had SRB and died. One of the

men with SRB who died abruptly and unexpectedly shortly after we had examined him had clinical evidence only of hypertensive cardiovascular disease, and another had clinical evidence only of chronic bronchitis and emphysema. However, an autopsy on the first of these men showed that he did, in fact, have extensive coronary atherosclerosis, as well as left ventricular hypertrophy; no autopsy was performed on the second man.

If sustained relative bradycardia is an indication of a disorder of the cardiac pacemaker, there remains the question of why this disorder of the pacemaker occurs. A most reasonable first assumption is that it is a manifestation of underlying heart disease. Disorders of the cardiac pacemaker occur not infrequently in association with this disease.[17-21] Although not all of our subjects had overt coronary heart disease or clinical evidence of coronary heart disease prior to sudden deaths, it is, nevertheless, quite possible that they did have much atherosclerosis of their coronary vessels. Experience up to now indicates that a large proportion of people who die unexpectedly without an obvious explanation have extensive coronary atherosclerosis at autopsy.[22,23] Atrial infarctions and occlusions of the vessels that supply the sinus node are apparently more common than is usually appreciated.[21]

However, this may not be the entire explanation. Sustained relative bradycardia was observed to occur frequently in association with pulmonary disease and hypertensive cardiovascular disease in people who had no clinical evidence of coronary heart disease and few of the standard risk factors such as diabetes or hypercholesterolemia. People with pulmonary disease often have dysrhythmias and disorders of cardiac conduction apparently as a concomitant of their pulmonary disease.[24] It seems quite possible that there may be people in the adult population who have sustained relative bradycardia with disease of the pacemaker and conduction system, which is not based upon coronary atherosclerosis. It has been suggested that degeneration of the pacemaker and conduction system may occur independently in some people[25-27] or in association with the aging process.[16]

There seems to be no paradox in the fact that sustained relative bradycardia was significantly related to the occurrence of subsequent deaths not reported as coronary deaths. The relationship of SRB to these deaths appears to arise from its relationship to the presence of diseases—hypertension, pulmonary disease, and atherosclerosis—which carry with them the increased risk of death regardless of the presence of sustained relative bradycardia. Seven of the 34 men with SRB were reported to have died of causes other than coronary heart disease. One of these was a man with hypertension and coronary heart disease who died of a stroke. Another, who also had hypertension and coronary heart disease, developed a gram-negative endocarditis after a prostatectomy and died with this as the precipitating cause. One man with SRB, who had hypertension, developed carcinoma of the prostate and during his terminal course went into congestive heart failure from which he died. Two men with SRB who had emphysema died of carcinoma of the lung; they were both heavy smokers. Two men with sustained relative bradycardia died of carcinoma of the cecum and carcinoma of the colon, respectively. Two deaths such as these might have been expected to occur in a sample of 34 men on a purely random basis; the fact that the men who died had sustained relative bradycardia may have been an incidental finding related to the fact that one of them had hypertensive cardiovascular disease with the LVH pattern, and evidence of an intraventricular conduction defect on his ECG, while the other had probable coronary heart disease with ischemic ST segments.

Although the relation of SRB to subsequent deaths from causes other than intrinsic heart disease appears to be explained by the fact that it occurs in association with diseases which carry with them an independent risk of mortality, the overall risk of death associated with the presence of sustained relative bradycardia cannot be explained in this manner. The presence of SRB increased the risk of death among men who had hypertension with or without LVH patterns on the ECG; and it increased the risk of death among men with pulmonary disease. Sustained relative bradycardia appears to have made a significant and independent contribution to the likelihood of death of men in this sample.

From a prognostic point of view, the greatest importance of SRB appears to lie in its ability to identify men with a high likelihood of sudden and unexpected death whether or not these men have overt evidence of coronary heart disease at the time of the examination. Three of the six men who had SRB and who subsequently died abruptly and unexpectedly did not have definite or probable evidence of coronary heart disease when the SRB was first detected. Conversely, five of the ten men in the sample who did not have overt clinical evidence of coronary heart disease at the time of the first examination, and who later died within less than one hour after the onset of the fatal episode, had sustained relative bradycardia at the first examination.

## Conclusions

During a prospective study of a random sample of 301 actively employed middle-aged men, who were observed over a seven-year period and were between the ages of 55 and 65 years, there were found to be 34 men who had slow heart rates, sustained throughout a carefully standardized six-hour routine of ordinary activity at the time of the first examination. The sustained slow heart rates were characterized by a mean afternoon heart rate of 70 beats per minute or less, or a mean afternoon heart rate of 80 beats per minute or less, provided the afternoon heart

rate was not more than 15 beats per minute greater than the morning supine heart rate. We have referred to this as a "sustained relative bradycardia."

The presence of such a sustained slow heart rate was significantly associated with the presence of definite or probable coronary heart disease, and it was often found in association with definite hypertension or pulmonary disease, or some combination of these three conditions.

Sustained relative bradycardia was significantly associated with preexisting evidences of disorders of the cardiac pacemaker and it was often followed by the development of new evidence of disorders of the pacemaker. Men who had SRB often had disorders of their cardiac conduction systems also, but these did not appear to account for the occurrence of the slow heart rate.

Men with sustained relative bradycardia, as we have defined it, experienced a significantly greater proportion of subsequent acute cardiac deaths than other men in the sample. They also experienced a greater proportion of abrupt and unexpected deaths. Men with sustained relative bradycardia accounted for approximately one third of the subsequent acute cardiac deaths and for one third of the sudden and unexpected deaths that occurred.

The finding of a sustained relative bradycardia in middle-aged men who have evidence of coronary heart disease, hypertensive cardiovascular disease or pulmonary disease, especially if they also have evidence of abnormalities of the cardiac pacemaker and conduction system, suggests that the risk that these men will experience acute cardiac death within the next five years is significantly greater than that of otherwise similar men without these abnormalities.

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